REMARKS

Applicant respectfully requests reconsideration. Claims 92-104, 106-109, 111, 112, 114, 115 and 117-130 are pending in this application with claims 92 and 104 being independent claims. Claims 92-104, 106-109, 111, 112, 114, 115 and 117-130 have been amended. No new matter has been added.

Claim Objections

The Examiner objected to claim 92 because of two occurrences of "and". Applicant has amended claim 92 and removed the "and" in line 17. The Examiner objected to claim 92 because of the duplicate recitation of "one". Applicant has amended claim 92 such that "one" is no longer recited in duplicate.

The Examiner objected to claim 104 because of a misplaced "and". Applicant has amended claim 104, with "and" now preceding the last method step. The Examiner also objected to claim 104 because of a lack of antecedent basis for "said differentiated somatic cell" and "said differentiated somatic cells". Applicant has amended claim 104 such that antecedent basis is provided.

Accordingly, reconsideration and withdrawal of the claim objections are respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 92-104, 106-109, 111, 112, 114, 115 and 117-130 under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement. According to the Examiner, (1) at the time of filing, the art taught unpredictable results in the cloning of primates, (2) the claims encompass cross-species nuclear transfer, (3) the degree of experimentation for the breadth of any differentiated cell is unpredictable, and (4) operable linkage to a promoter or expression regulatory sequence is necessarily required for an enabled use.

Applicant respectfully traverses. First, Applicant maintains that at the time of filing, contrary to the Examiner's assertion, the cloning of primates was enabled, as was discussed in the response to the previous office action. For example, Meng et al. (Biol. Reprod. 1997, 2:454),

teach a method for the generation of rhesus monkeys by nuclear transfer, while Chan et al. (Science 2001, 291:309), teach the production of transgenic rhesus monkeys. Furthermore, even if some embodiments of the claims are inoperable, which the Applicant does not concede is the case, the presence of such embodiments does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments would be inoperative or operative with the expenditure of no more effort than is normally required in the art. (MPEP §2164.08). Therefore, even if, *arguendo*, the cloning of primates is inoperable, a person of ordinary skill in the art could determine so with no more than routine experimentation. No undue experimentation would be required.

Second, in regard to cross-species nuclear transfer, without conceding the correctness of the Examiner's position and merely in the interest of expediting prosecution, Applicant has amended independent claims 92 and 104 to reflect that the cells or cell-lines and the mammals are of the same species.

Third, Applicant respectfully traverses the Examiner's contention that for the breadth of any differentiated somatic cell, the degree of experimentation is unpredictable. The claims are enabled for the production of transgenic animals using any differentiated somatic cell. The Examiner refers to Clark et al. and Denning et al. to support the argument that obtaining a fibroblast culture of primary cells is challenging. In contrast to the interpretation by the Examiner, Clark et al. and Denning et al. actually provide support for the enablement of the use of any somatic cell including cultured fibroblasts in nuclear transfer. Both Clark et al. and Denning et al. show that a fibroblast culture of transgenic cells can be established prior to senescence. In addition, Clark et al. state that "populations of senescent donor somatic cells can be used" (See, e.g., page 268, column 2, line 10). Thus, nuclear transfer can be performed with senescent cells. There is no requirement for selection prior to senescence as asserted by the Examiner. In addition, Clark et al. provide a variety of different somatic cell types, including fibroblasts, cumulus cells, muscle cells and cells of the mammary epithelia that have been used for cloning in a variety of animal species (See, e.g., page 265). Thus, Clark et al. and Denning et al. teach that cultures of primary transfected cells can be established, senescent cells can be used for nuclear transfer, and a variety of somatic cells can be used for cloning.

In regard to the enablement for nuclear transfer when a neural cell is the nuclear donor, the Examiner has argued that the teachings of Wakayama et al. demonstrate that neural cells cannot be used for nuclear transfer. However, a literature reference published at a later date than the Wakayama reference, but prior to the filing of the instant application, shows that the use of neuronal cells for nuclear transfer had been established (See, e.g., Kawase et al. Genesis 2000, Nov-Dec; 28 (3-4) 156-163 (abstract)). Furthermore, as argued above, even if some embodiments of the claims are inoperable, which the Applicant does not concede is the case, the presence of such embodiments does not necessarily render a claim nonenabled. Again, the standard is whether or not one of ordinary skill in the art would require undue experimentation to determine which embodiments are inoperative. This has not been established.

Finally, the Examiner states that operable linkage of a DNA sequence encoding a protein to a promoter or expression regulatory sequence is required to "enable use". However, the Examiner does not explain how this statement relates to, or supports, the enablement rejection. Nevertheless, without conceding that the Examiner is correct, and in the interest of expediting prosecution, Applicant has amended claim 92 to state that the DNA sequence is operably linked to a promoter. Further, Applicant notes that claim 104 recites that the desired gene is actuated by a tissue-specific promoter.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

<u>Rejections under 35 U.S.C. §112, first paragraph</u>

The Examiner rejected claim 92 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Examiner, the metes and bounds of the term "molecular biology methods" are unclear.

Without conceding the correctness of the Examiner's position and merely in the interest of expediting prosecution, Applicant has amended claim 92 to remove the recitation of "molecular biology methods".

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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1: Genesis. 2000 Nov-Dec;28(3-4):156-63.

Mouse embryonic stem (ES) cell lines established from neuronal cell-derived cloned blastocysts.

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We have established mouse embryonic stem (ES) cell lines from blastocysts derived by transfer of nuclei of fetal neuronal cells. These neuronal cell-derived embryonic cell lines had properties that characterize them as ES cells, including typical cell markers and alkaline phosphatase activity. Moreover, the cells had a normal karyotype and were pluripotent, as they were capable of differentiating into all three germ layers. Although they were derived from neuronal donor nuclei, the cells no longer expressed neuronal markers; however, they were capable of differentiating into cells with neuronal characteristics. These results suggest that the clone-derived cells have fully acquired an ES cell character. Thus, ES cells can be derived from embryos resulting from nuclear transfer, which results in reprogramming of the genetic information and acquisition of pluripotency. ES cells established from somatic cell-derived blastocysts could be useful not only as research tools for studying reprogramming but also as models for cell-based transplantation therapy.

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